jection, we hypothesized that atherothrombotic risk factors may contribute to accelerated atherosclerosis. We therefore prospectively evaluated the burden of coronary atherosclerosis by intravascular ultrasound (IVUS) in 20 patients and measured plasma fibrinogen (FGN), lipoprotein (a) (Lp(a)) and net fibrinolytic activity of plasma using a standard fibrin plate assay. Intimal thickening was quantified using IVUS by measuring the intimal index (Ii = intimal area/[intimal area + luminal area]) in 2–5 segments of the LAD using planimetry. The maximal Ii per patient was calculated and indexed to the time post-transplant (MxIi/Yr). FGN predicted severity of MxIi/Yr (r^2 = 0.41, p = 0.008). In patients with decreased plasma fibrinolytic activity (lytic zone < 100 mm^2), MxIi/Yr was increased ten-fold (0.21 ± 0.17 vs. 0.02 ± 0.02, p = 0.002). Because Lp(a) colocalizes with fibrinogen in the vessel wall and inhibits fibrinolysis, we correlated plasma Lp(a) levels with the degree of intimal thickening. Lp(a) did not predict MxIi/Yr (p = NS). In conclusion, these data suggest that plasma FGN and net fibrinolytic activity predict the degree of intimal thickening and that fibrin deposition may play an integral role in diffuse coronary atherosclerosis after cardiac transplantation.

936-87 Serial Dobutamine Stress Echocardiography for Detection of Cardiac Allograft Vasculopathy

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Dobutamine stress echocardiography (DSE) is a noninvasive and safe test to detect myocardial ischemia. To analyse, if DSE is feasible for assessment and follow up of coronary allograft vasculopathy (CAV), 13 patients (P, 50 +/= 8 years, 60 +/= 32 months after heart transplantation) were studied at 2 consecutive routine annual investigations by coronary angiography (ANGIO), intravascular ultrasound (IVUS quantitative analysis of degree and extension of intimal hyperplasia; modified Stanford grading, grades 1–6) and dobutamine stress echocardiography (DSE, 5–40 mcg/kg/min, 5 min stages). Regional wall motion abnormalities (WMA) were assessed qualitatively (2-D-echo, 16 segment model) and quantitatively (M-Mode, systolic thickening of interventricular septum (IVS) and LV posterior wall (LPW)).

Results: P were allocated to 2 groups: group 1, normal DSE at entry (n = 9); group 2, WMA during DSE at entry (n = 4). At the initial study, no P had WMA at rest. In group 1, IVUS revealed only mild intimal hyperplasia (mean, < grade 3.5) in group-1 P; ANGIO was completely normal in 8/9 P and showed mild dilating angiopathy in 1/9 P. 4 group-2 P developed WMA during DSE (total, 12/64 segments); ANGIO was normal in all P, IVUS grades were 1.2/1.7/4.0/5.5. Mean systolic thickening of IVS (rest, 26 vs. 32%; max.DSE, 37 vs. 63%, group 2 vs. 1) and LPW (rest, 35 vs 57% max.DSE, 65 vs. 95%) were smaller in group 2 than in group 1. At follow up, 3/9 group-1 P had DSE-induced WMA (9/144 segments); all had IVUS progression to grade >3.5, but no ANGIO changes. In group 2, 1 P with stress induced WMA in only one segment at entry was judged normal at follow up (IVUS: 1.2 and 1.6, respectively; false positive DSE at entry). 3 group-2 P deteriorated: 1 had diffuse WMA at rest, all 3 had increasing WMA at DSE (total, 26/48 segments. Mean IVUS grades rose to 4.0/5.5/6.0; ANGIO remained normal in 2 P and showed diffuse rarefication of small vessels in 1 P.

Conclusion: All P with marked-to-severe intimal hyperplasia assessed by IVUS and/or marked ANGIO findings were identified by DSE. Serial DSE is a feasible and safe method for noninvasive screening and follow-up for CAV in heart transplant recipients. In P with normal DSE, the need for routine ANGIO at regular intervals may be reduced.

936-88 Relationship of Donor Age and Pre-existing Coronary Disease by Angiography and Intracoronary Ultrasound to Later Development of Cardiac Allograft Coronary Artery Disease

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The increasing demand for cardiac donors has led to a tendency to liberalize age and other criteria for donor acceptability. Since cardiac allograft coronary artery disease (TxCAD) is the major complication limiting longterm post-transplant survival, we analyzed a series of 242 consecutive cardiac transplant patients (Tx pts) who had baseline early post-op coronary angios and a subset of 41 pts with baseline intracoronary ultrasound (ICUS) to determine whether either older donor age or pre-existing CAD at the time of transplant influenced the later occurrence of TxCAD.

Fourteen pts had angiographic evidence of some pre-existing CAD (donor CAD group); the other 228 did not (no donor CAD group). New disease was defined as either development of new obstructive lesions or progression of old lesions on serial annual angios. Freedom from new disease was 86%, 71%, and 30% at 1, 2, and 3 years post-op in the donor CAD group and 97%, 89%, and 77% in the no donor CAD group (p = 0.003). No donor CAD pts were subdivided into older (≥40) and younger (<40) groups. Freedom from TxCAD was 92%, 52%, and 43% at 1, 3, and 5 years post-op in the older group (n = 31, mean age 49) vs. 97%, 82%, and 53% in the younger group (n = 184, mean age 24) p = 0.03 (Mantel-Haenszel).

Baseline ICUS imaging revealed baseline class 3 or 4 lesions in 7 of 9 older donor hearts, and in only 7 of 32 younger hearts (p = 0.006). Three of these 14 ICUS class 3/4 pts later developed TxCAD vs. only 3 of 27 class 1/2 pts at baseline (p = NS). Older donor age, no calcium blocker use and pre-existing CAD were significant predictors for development of TxCAD (p = 0.0006, 0.0003, and 0.003 respectively, Cox regression analysis).

Conclusion: (1) Older donors or pre-existing CAD have a greater tendency to develop TxCAD, (2) ICUS reveals moderate to severe intimal thickening not angiographically detectable and there is a trend toward such disease leading to later TxCAD.

936-89 Extent of Coronary Myointimal Proliferation and its Relationship to Resistance Vessel Function in the Cardiac Allograft

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Transplant coronary arteriopathy is the major obstacle to long-term survival of cardiac allografts and is characterized by myointimal proliferation involving both epicardial conduit vessels and intramyocardial resistance vessels. To evaluate the relationship between conduit disease and resistance vessel integrity, 70 coronary arteries in 58 transplant patients were studied with a 3.5 Fr 30 MHz intravascular ultrasound (IVUS) probe and an 0.018" doppler guidewire. Epicardial conduit disease was characterized by the presence or absence of IVUS discernible intimal thickening, (>500 microns or <500 microns) in either a diffuse (trilaminar appearance along whole course of studied segment) or a focal (with areas of vessel free of intimal thickening) distribution. Resistance vessel function was assessed by measuring coronary flow reserve (CFR = maximal hypermic/resting blood flow velocity) using intracoronary adenosine (18 mg). *Results* (means ± SD):

	None (n = 12)	Diffuse > 500 (n = 19)	Diffuse < 500 (n = 18)	Focal > 500 (n = 7)	Focal < 500 (n = 14)
CFR	3.1 ± 0.5	3.3 ± 0.4	3.7 ± 0.7	2.3 ± 0.6*	2.8 ± 4*

p < 0.01 vs diffuse

There were no differences in the CFR between arteries with (n = 58) and without (n = 12) intimal thickening (3.2 ± 0.6 vs 3.1 ± 0.5; p = NS) or based on the maximal thickness of the intima (<500 microns, 3.2 ± 8 vs >500 microns 3.0 ± 0.7, p = NS). Extensive myointimal thickening can occur without diminishment of the CFR. Focal intimal disease is associated with a significantly more profound effect on microvascular function then classically described diffuse disease. This suggests that typical epicardial transplant arteriopathy can occur without involvement of small vessels.

936-90 Impact of Ischemia Time on Vascular Rejection and Expression of Peptide Growth Factors in Transplant Arteriosclerosis

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Accelerated arteriosclerosis in transplanted organs represents the major cause of graft failure and is limiting the clinical outcome of heart transplantation.

Using a rat aorta transplant model the impact of cold ischemia time up to 24 hours (extracorporal storage time) and reperfusion injury upon development of transplant arteriosclerosis was analysed during the first 2 months after transplantation both in allogeneic as well as in syngeneic transplants. The expression of the various isoforms of transforming growth factor-β (TGF-β), latent TGF-β binding protein (LTBP) as well as platelet-derived growth factor (PDGF) and its receptors were studied using immunohistochemistry, followed by a semi-quantitative evaluation and multivariant analysis (n = 18 for each antiserum).

In the syngeneically transplanted aortas the expression of TGF-β1 (p < 0.03), PDGF-BB (p < 0.05) and of the PDGF α-receptor (p < 0.03) in the neointima increased significantly with the extent of cold ischemia time. Furthermore, there was a significant induction of LTBP (p < 0.05) correlating with the observation time after transplantation. In the allogeneic aortic grafts, expression of all examined proteins was increased soon after transplantation.

In summary, TGF-β and PDGF are induced by allogeneic as well as ischemic stimuli in transplanted vessels. Moreover, in the syngeneic transplantation model, cold ischemia time prior to implantation has an impact on the expression of growth factors and the extent of vascular remodeling.